

In the Claims:

Please cancel claims 4-6, 15-18, 21-36, 43-47, 50-51, 53-54, 56-59, and 61-67 without prejudice to Applicant.

Please amend claim 20 as indicated below in the complete claim listing.

The complete listing of all claims pursuant to 37 C.F.R. § 1.121(c) follows below:

1. (Original) A method for treating a disease or condition associated with the activity of a G protein coupled receptor (GPCR) comprising administering an inverse agonist for the GPCR to an organism with a disease or condition associated with the activity of the GPCR in a quantity and for a period that causes an increase in the population of GPCRs, either spontaneously active or those that are available and activated by an endogenous agonist or by an exogenous agonist, associated with that physiological function, thereby producing a therapeutic effect to ameliorate the disease or condition.

2. (Original) The method of claim 1 wherein the administration of the inverse agonist results in continuous levels of the inverse agonist in the bloodstream of the organism to which the inverse agonist is being administered.

3. (Original) The method of claim 1 wherein the disease or condition associated with the activity of a GPCR is a pulmonary airway disease.

4.-6. (Cancelled).

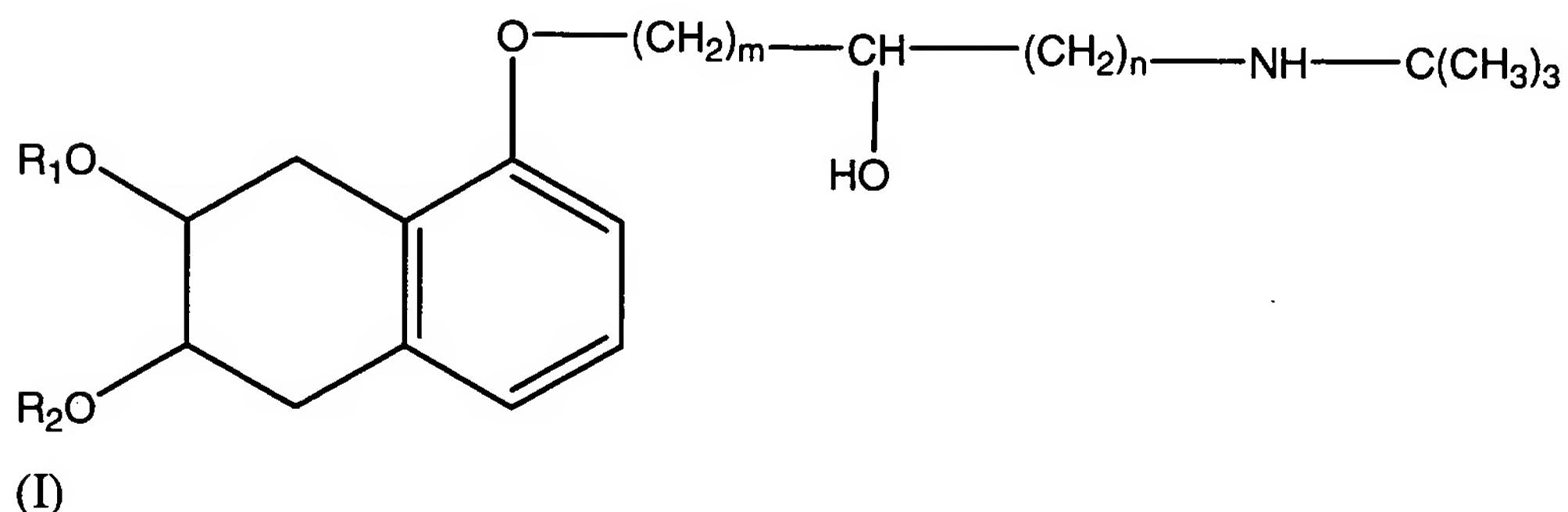
7. (Original) The method of claim 3 wherein the GPCR is a β_2 -adrenergic receptor.

8. (Original) The method of claim 7 wherein the therapeutic effect is an upregulation of the population of pulmonary β_2 -adrenergic receptors.

9. (Original) The method of claim 7 wherein the therapeutic effect is increased pulmonary airway relaxation responsiveness to β_2 -adrenergic agonist drugs.

10. (Original) The method of claim 7 wherein the inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, and timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

11. (Original) The method of claim 10 wherein the β -adrenergic inverse agonist is selected from the group consisting of nadolol and a compound of formula (I)

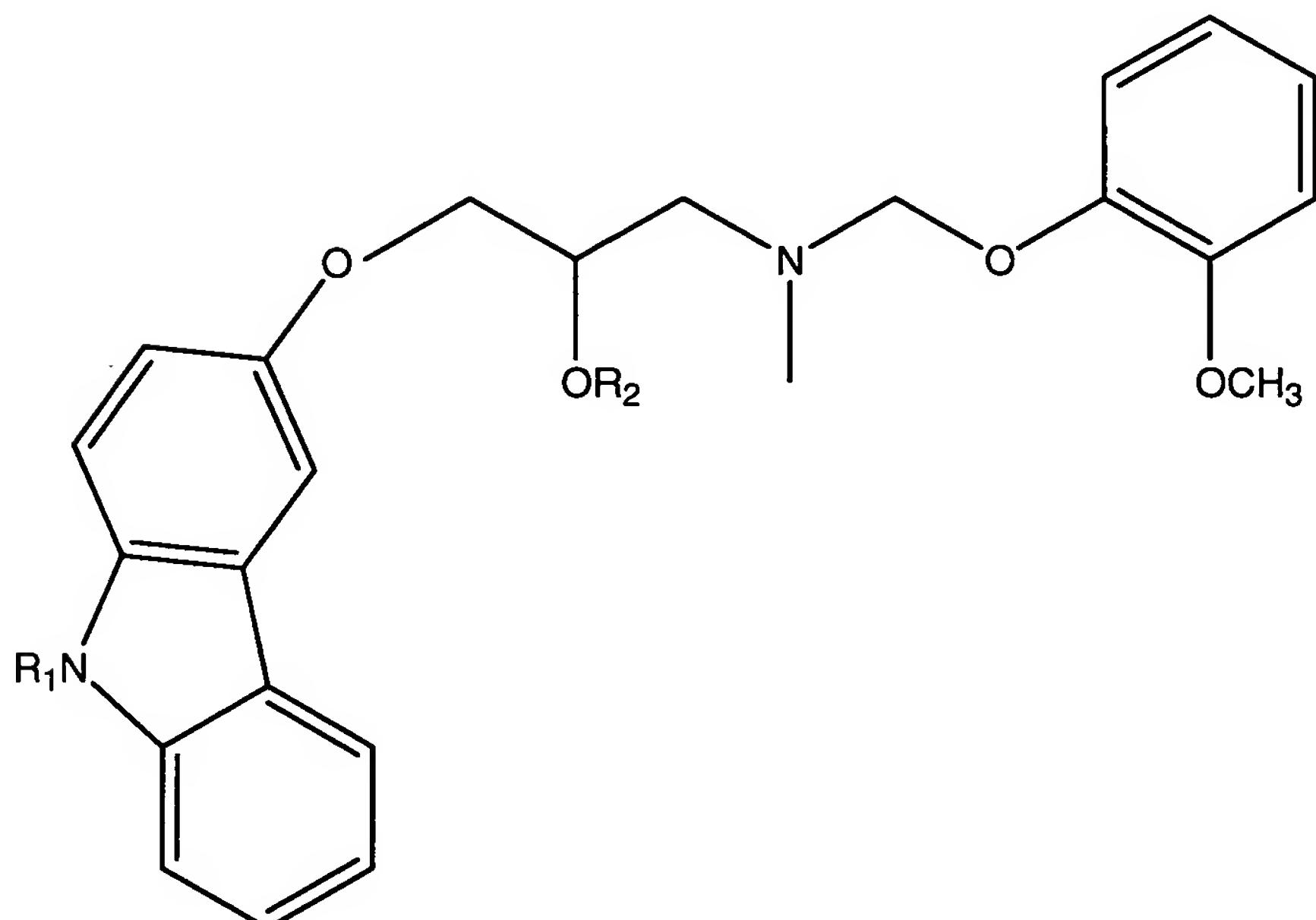


(I)

wherein R₁ is hydrogen or lower alkyl, R₂ is hydrogen or lower alkyl, and m and n are 1 to 3, with the proviso that where R₁ and R₂ are both hydrogen and m is 1, n is other than 1.

12. (Original) The method of claim 11 wherein the β -adrenergic inverse agonist is nadolol.

13. (Original) The method of claim 10 wherein the β -adrenergic inverse agonist is selected from the group consisting of carvedilol and a compound of formula (II)



(II)

wherein R₁ is hydrogen or lower alkyl, R₂ is hydrogen or lower alkyl, and R₃ is hydrogen or lower alkyl, with the proviso that all of R₁, R₂, and R₃ are not all hydrogen.

14. (Original) The method of claim 13 wherein the β -adrenergic inverse agonist is carvedilol.

15.-18. (Cancelled).

19. (Original) The method of claim 3 wherein the method further comprises the administration of an additional agent.

20. (Currently amended) The method of claim 19 wherein the additional agent is selected from the group consisting of a β_2 -selective adrenergic agonist drug, a

steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase IV inhibitor.

21.-36. (Cancelled).

37. (Original) The method of claim 1 wherein the disease or condition associated with the activity of a GPCR is congestive heart failure (CHF).

38. (Original) The method of claim 37 wherein the GPCR is a β_2 -adrenergic receptor.

39. (Original) The method of claim 38 wherein the inverse agonist is nadolol.

40. (Original) The method of claim 1 wherein the GPCR is selected from the group consisting of acetylcholine receptors, α -adrenergic receptors, β_3 -adrenergic receptors, serotonin (5-hydroxytryptamine) receptors, dopamine receptors, adenosine receptors, angiotensin Type II receptors, bradykinin receptors, calcitonin receptors, calcitonin gene-related receptors, cannabinoid receptors, cholecystokinin receptors, chemokine receptors, cytokine receptors, gastrin receptors, endothelin receptors, γ -aminobutyric acid (GABA) receptors, galanin receptors, glucagon receptors, glutamate receptors, luteinizing hormone receptors, choriogonadotrophin receptors, follicle-stimulating hormone receptors, thyroid-stimulating hormone receptors, gonadotrophin-releasing hormone receptors, leukotriene receptors, Neuropeptide Y receptors, opioid receptors, parathyroid hormone receptors, platelet activating factor receptors, prostanoid (prostaglandin) receptors, somatostatin receptors, thyrotropin-releasing hormone receptors, vasopressin and oxytocin receptors.

41. (Original) The method of claim 40 further comprising administering an agonist to the GPCR.

42. (Original) A method for screening a compound for inverse agonist activity against a GPCR comprising the steps of:

- (a) providing a population of specific G protein coupled receptors characterized by a constitutive basal level of activity in the absence of an agonist;
- (b) contacting the population of specific G protein coupled receptors with a compound to be screened for its inverse agonist activity, the compound not being an agonist of the population of specific G protein coupled receptors; and
- (c) determining the constitutive basal level of activity of the specific G protein coupled receptors in the absence of the compound and in the presence of the compound, such that the constitutive basal level of activity decreases if the compound is an inverse agonist.

43.-47. (Cancelled).

48. (Original) The method of claim 42 wherein a physiological consequence of receptor activation is measured.

49. (Original) The method of claim 48 wherein the physiological consequence of receptor activation is airway resistance.

50.-51. (Cancelled).

52. (Original) A method for screening a compound for inverse agonist activity against a GPCR comprising the steps of:

- (a) providing cells containing a population of specific G protein coupled receptors characterized by a constitutive basal level of activity in the absence of an agonist;
- (b) contacting the cells containing the population of specific G protein coupled receptors with a compound to be screened for its inverse agonist activity, the

compound not being an agonist of the population of specific G protein coupled receptors, the compound being contacted with the cells for a period of time to result in an increase in receptor population or receptor density if the compound is an inverse agonist; and

(c) determining the receptor population or receptor density of the specific G protein coupled receptors in the cells in the absence of the compound and in the presence of the compound, such that the receptor population or receptor density increases if the compound is an inverse agonist.

53.-54. (Cancelled).

55. A method for treating a disease or condition associated with the activity of a G protein coupled receptor (GPCR) comprising administering an inverse agonist for the GPCR to an organism with a disease or condition associated with the activity of the GPCR in a quantity and for a period that prevents the decrease in the population of GPCRs due to the presence of either exogenous or endogenous agonist, thereby producing a therapeutic effect to ameliorate the disease or condition.

56.-59. (Cancelled).

60. (Original) A pharmaceutical composition comprising:

(a) a therapeutically effective amount of an inverse agonist for a GPCR;
(b) a therapeutically effective amount of a second therapeutic agent, the second therapeutic agent being selected from the group consisting of a β_2 -selective adrenergic agonist, a steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase IV inhibitor; and
(c) a pharmaceutically acceptable carrier.

61.-67. (Cancelled).